

ABSTRACT

This invention provides immunologically compatible animal tissue, suitable for xenotransplantation into human patients. Sequence of the cDNA for the sheep
5 $\alpha(1,3)$ galactosyltransferase has been determined, along with information about the flanking untranscribed regions and introns of the $\alpha 1,3$ GT gene. This in turn has led to the design and implementation of targeting vectors capable of inactivating the $\alpha 1,3$ GT gene by deleting or interrupting the protein coding region. Successfully targeted fibroblasts are used as nuclear donors for the cloning of animals in which the $\alpha 1,3$ GT gene is inactivated. The Gal $\alpha(1,3)$ Gal
10 determinant does not form on endothelial and other cells of animals having homozygously inactivated $\alpha 1,3$ GT. The tissues can be transplanted into human patients, without being subject to hyperacute rejection that would otherwise occur due to naturally occurring antibodies to the Gal $\alpha(1,3)$ Gal determinant present in human serum. Because of the limited availability of human organs for transplantation, immunologically compatible animal tissue is
15 an important alternative for human organs that are in such short supply for transplantation therapy.